Evaluation of disease spectrum diagnosed with bone marrow biopsy at a tertiary healthcare center in Turkey

Hematological diseases spectrum diagnosed with bone marrow biopsy

Ahmet Seyhanlı[1], Yazgulu Cansu Ozkan[2], Sermin Ozkal[3], Guner Hayri Ozsan[4], Fatih Demırkan[4], Inci Alacacıoglu[4]
[1] Department of Hematology, Sivas Numune Hospital, Sivas
[2] Department of Internal Medicine, Dokuz Eylül University Faculty of Medicine, Izmir
[3] Department of Pathology, Dokuz Eylül University Faculty of Medicine, Izmir
[4] Department of Hematology, Dokuz Eylül University Faculty of Medicine, Izmir, Turkey

Abstract
Aim: Bone marrow examination (BME) is commonly implemented to diagnose hemato-oncological diseases. There are only a few reports on diseases diagnosed via the BME and diagnostic yield in patients who applied to the hematology department. This study aimed to identify the primary indications and diagnoses of BME in patients who underwent bone marrow biopsy at Dokuz Eylul University in Turkey.
Material and Methods: We retrospectively reviewed demographic and laboratory data of 505 patients from January 2014 to September 2021. The cases under the age of 18 years were excluded. The patients were also stratified according to demographic data and diagnoses.
Results: Among the 505 bone marrow biopsies (BMB) studied, 386 (76.4%) procedures were performed to evaluate suspected malignancy and 119 (23.6%) for non-malignant indications. The primary indications for BME were: cytopenia (117, 23.2%), plasma cell neoplasm (PCN) (94, 18.6%), and myeloproliferative neoplasms (93, 18.4%). The most common diagnoses among all patients were PCN (110, 21.8%). Non-malignant outcomes comprised 3.2% of the total outcomes with 16 cases, of which thrombocytopenia due to peripheral destruction (immune thrombocytopenia) was the most common with eight (1.6%) patients. The majority of patients diagnosed with myelodysplastic syndrome and CLL were seen in patients aged 65 years and older.
Discussion: There is little published literature on the bone marrow profile, especially in geriatric patients. The higher incidence of hematological diseases in patients under 65 years of age can be attributed to more common BME procedures, which leads to earlier diagnosis.

Keywords
Hematologic Diseases, Trephine Biopsy, Bone Marrow

Introduction

The bone marrow examination (BME) is commonly implemented to diagnose hemato-oncological diseases. Aspiration of the cellular component, bone marrow biopsy (BMB), or both are used for BME. BMA provides cellular material for cytogenetic and molecular evaluation, microbiologic cultures, and flow cytometry. BMB enables evaluating the cellularity, finding focal lesions, and establishing the diagnosis of infiltrated bone marrow by various pathologic conditions. Most BMEs are performed on the posterior superior iliac spine (PSIS) in adults. The World Health Organization recommends a minimum of 1.5 cm long biopsy specimen for diagnosis [1]. BME is a low-risk invasive procedure but not entirely free of risk; the British Society of Hematologists reported a severe adverse event rate ranging from 0.05% to 0.12%. Hemorrhage was the most commonly reported adverse event. Prolonged severe pain, nerve compression, pelvic fractures, and sepsis indirectly attributable to the procedure were also reported [2,3]. Therefore, a real diagnostic approach is required. The most common reasons for BME have been for the diagnosis of hematological malignancies [4,5]. The diagnostic spectrum via BME at our institution has not been previously studied in Turkey. We evaluated the indications and diagnostic yields of BME at the Dokuz Eylul University Hospital in Turkey.

Material and Methods

We analyzed the BME results of 505 patients (18 years or older) between January 2014 and September 2021 in the outpatient and inpatient hematology service at Dokuz Eylul University Hospital in Turkey. Ethical clearance was obtained from our local ethics committee. The demographic and clinical data, laboratory parameters of the patients were retrospectively evaluated. After obtaining informed consent, we performed the procedure with local anesthesia to the PSIS. Most of the procedures consisted of aspiration and biopsy. However, we did not analyze the results of aspiration in the present study and only evaluated BMB indications and diagnosis in the proper groups for comparison. This study was approved by the Ethics Committee of Dokuz Eylul University (Approval date: 29.03.2021, Issue number: 2021/10-48).

Statistical analysis

Data were analyzed using SPSS 24.0 software (IBM SPSS Inc, Chicago, IL, USA). Numerical variables were presented as median/mean ±standard deviation, and categorical variables were presented as number (n) and percentage (%).

Results

The median age was 62 (20-90) years. Among the 505 patients, 300 (59.4%) were men, and 205 (40.6%) were women. Of these 505 BMB studied, 386 (76.4%) procedures were performed to evaluate suspected malignancy and 119 (23.6%) for non-malignant indications. The primary indications for BME were cytopenia 117 (23.2%), plasma cell neoplasm (PCN) 94 (18.6%), and myeloproliferative neoplasms 93 (18.4%). Indications for BME procedures are shown in Table 1.

In 500 patients (99%), BME was diagnostic or provided useful information for diagnosis. The most common diagnoses among all patients were 110 (21.8%) PCN and 95 (18.8%)

myeloproliferative neoplasm (MPN) infiltration cases. Other common diagnoses were 78 cases (15.4%) of non-Hodgkin lymphoma and 55 cases (10.9%) of myelodysplastic syndrome (MDS), and 46 cases (9.1%) of acute leukemia. Among the acute leukemias, 28 had acute myeloid leukemia, and 18 had acute lymphoid leukemia confirmed through flow cytometric immunophenotyping or immunohistochemistry. There were 19 (3.8%) cases of non-hematological disorders, including 18 (3.6%) metastatic deposits and one case of bone marrow tuberculosis granuloma. Of the 18 solid tumor metastases, seven cases had bone marrow involvement of prostate cancer, and six cases had bone marrow involvement of breast cancer. The patient diagnosed with gastric adenocarcinoma had no history of malignancy, and BME was applied to examine pancytopenia. Non-malignant outcomes were observed in 16 cases and comprised 3.2% of the total outcomes, of which thrombocytopenia due to peripheral destruction (immune thrombocytopenia) was the most common in 8 (1.6%) cases. Twenty cases (4%) were classified as normal bone marrow results, and five (1.0%) sample materials were insufficient for a definite opinion. The disease spectrum diagnosed with BME is given in Table 2.

We divided the patients into two groups according to age groups: under 65 years of age and 65 years old and over. Most of the patients diagnosed with myeloproliferative neoplasia and Hodgkin lymphoma were seen in the group under 65 years of age. The majority of patients diagnosed with myelodysplastic syndrome and CLL were seen in 65 and above. The number and percentage of the diagnosis of patients are given in Table 3.

Table 1. Indications for performing bone marrow trephine biopsies

Indications	n	%
Non-malignant indications		
Anaemia	25	5
Thrombocytopenia	11	2.2
Leukopenia	4	0.8
Bicytopenia	35	6.9
Pancytopenia	42	8.3
Granulomas-others	2	0.4
Total number of non-malignant indications	119	23.6
Malignant indications		
Lymphoma		
Non-Hodgkin's Lymphoma	71	14.1
Hodgkin's lymphoma	6	1.2
Leukaemia		
Acute myeloid leukaemia	29	5.7
Acute leukaemia non-specific	12	2.4
Chronic myeloid leukaemia	40	7.9
Chronic lymphocytic leukaemia	16	3.2
Plasma cell neoplasm	94	18.6
Myeloproliferative Neoplasms	93	18.4
Myelodysplastic syndrome	10	2
Bone Marrow Metastasis of Solid Tumors	15	3
Total number of malignant indications	386	76.4
Total	505	100

Table 2. Diseases diagnosed on morphological examination of bone marrow samples

Outcomes	n	%
Non-malignant outcomes		
Aplastic anemia	5	1
Pure red cell aplasia	1	0.2
Megaloblastic anemia	1	0.2
Thrombocytopenia due to	8	1.6
Peripheral destruction		
Granulomas-others	1	0.2
Malignant outcomes		
Non-Hodgkin's Lymphoma	78	15.4
Hodgkin's lymphoma	8	1.6
Acute leukaemia	46	9.1
Acute leukaemia non-specific	18	3.6
Chronic myeloid leukaemia	36	7.1
Chronic lymphocytic leukaemia	18	3.6
Plasma cell neoplasm	110	21.8
Polycythaemia vera	11	2.2
Essential thrombocytosis	49	9.7
Primary myelofibrosis	35	6.9
Myelodysplastic syndrome	55	10.9
Bone Marrow Metastasis of Solid Tumors	18	3.6
Non-specific findings/Normal	20	4.0
Inadequate	5	1.0
Total	505	100

Table 3. Malignant disease distributions by age groups

Malignant outcomes	AGE < 65 n (%)	AGE>65 n (%)
Non- Hodgkin lymphoma	43 (9.3)	35 (7.5)
Hodgkin lymphoma	6 (1.3)	2 (0.4)
Plasma cell neoplasm	59 (12.7)	53 (11.4)
Acute myeloid leukemia	16 (3.4)	11 (2.4)
Acute leukaemia non-specific	7 (1.5)	10 (2.2)
Myelodysplastic Syndrome	20 (4.3)	35 (7.6)
Polycythaemia vera	6 (1.3)	5 (1.1)
Essential thrombocytosis	28 (6.0)	21(4.5)
Primary myelofibrosis	22 (4.7)	13 (2.8)
Chronic myeloid leukaemia	26 (5.6)	10 (2.2)
Chronic lympocytic leukemia	5 (1.1)	13 (2.8)
Solid Tumor	12 (2.6)	6 (1.3)
Total	250 (53.8)	214 (46.2)

Discussion

BME is a critical implementation for diagnosing and monitoring hemato-oncological diseases and involves aspiration of the bone marrow cellular component and BMB for obtaining tissue fragments. BMB allows assessment of the marrow's cellularity, the presence of focal lesions, and establishing the diagnosis of infiltrated bone marrow due to various pathologic conditions such as lymphoma, granulomas, and solid metastatic tumor [6,7]. The procedure also allows the assessment of bone marrow-ablative chemotherapy and monitors the recovery process in patients undergoing bone marrow transplantation

[8,9]. BME is also part of the initial staging in patients with the newly diagnosed lymphoproliferative disease and chronic myeloid leukemia. Moreover, BME is essential to determine unexplained anemia, leukopenia, or thrombocytopenia, or the presence of blast or morphologically atypical cells in the peripheral blood smear. Most BMBs are performed on the PSIS in adults. Anterior superior iliac crest or anteromedial face of the tibia are other areas where BME is performed, especially in children. We performed all BMEs on the posterior superior iliac spine. The bone marrow biopsy is associated with anxiety. Reyhaneh Abbaszadeh et al. showed that smelling of lavender aroma is useful to reduce anxiety [10]. With increasing age, the hematopoietic system is modestly affected, and normal aging does not cause a considerable reduction in complete blood count (CBC) parameters [11-13]. Gulati et al. studied 83 patients aged 60 and above who underwent BME, observed a 44.6% prevalence of anemia, and did not find any case of MDS [14]. Likewise, Gaskell et al. showed that in patients aged 65 years and over, the prevalence of anemia was 40% (40–72%) among hospital admissions and 47% (31–50%) in those in nursing homes [15]. Patients 65 years and older are considered elderly patients. We found a 39.6% prevalence of anemia in elderly patients, similar to that reported by Gaskell et al.

Age is a significant risk factor for the development of hematological malignancies. The incidence of lymphoma, PCN, MDS, and MPN increases with age. In both groups, PCN was observed as the most common disease, followed by MPN. According to Palumbo et al., the median age of patients at diagnosis is nearly 66–70 years, with 37% of patients being less than 65 years old [16]. In our results, the number of PCN patients under 65 years of age was higher, although it was not statistically significant. Most cases of MPN are encountered in patients aged 40–60 years. The incidence of polycythemia vera in the United States is nearly 5–17 cases per 1 million population per year. However, the true incidences of essential thrombocythemia and myelofibrosis are unclear [17]. In our study, the evaluation of lymphoma bone marrow involvement constituted 15.6% of the BME indications, of which 14.1% were non-Hodgkin lymphomas, and 1.4% were Hodgkin lymphomas. Most BMEs in lymphoma cases were performed to stage the disease and to establish a treatment program. Michelle Margold et al. demonstrated that BMB is not necessary for the staging of patients presumed to have primary CNS lymphoma [18]. BME procedure was developed with the use of imaging guidance to increase the diagnostic yield [19]. Long et al. has reported a 95% diagnostic yield with an exact pathologic diagnosis of fluorine copy-guided BME administration [20]. Vadlamudi and Sterling reported adequate BME samples in 98.9% of their patients [21]. We had sufficient BME samples in 99% of our patients. On the other hand, many studies have shown that fluorine-18 fluorodeoxyglucose-positron emission tomography (PET/CT) scan is more helpful in evaluating bone marrow involvement, especially in patients with diffuse large B-cell lymphoma [22, 23]. Although the facility of PET-CT is available in our center, BME is routinely performed for disease staging in all lymphoma patients. Widespread use of PET/CT may reduce BME in lymphoma patients but requires more prospective studies to show the advantages of PET/CT scanning over BME

for all lymphoma patients.

The incidence of Hodgkin lymphoma shows a bimodal distribution, with the first peak occurring in young adults aged 15–34 years and the second peak in those aged >55 years [24]. The majority of our Hodgkin lymphoma patients were less than 65 years old; the median age was 40.2 (25–68) years. Chronic lymphocytic leukemia (CLL) is one of the most common types of leukemia in adults. In the present study, CLL constituted 3.9% of all patients. This low percentage is because CLL is usually diagnosed based on the evaluation of flow cytometry of the peripheral blood sample.

Our study had some limitations. The study did not include data from the pediatric population. In addition, we did not analyze the results of bone marrow aspiration and complications of the bone marrow procedure.

Conclusion

There is little published literature on the bone marrow profile, especially in geriatric patients. This is the first study, to the best of our knowledge, to evaluate the disease spectrum diagnosed through BMB by age groups in our region. Environmental factors can change the onset and age of the disease. The higher incidence of hematological diseases in patients under 65 years of age can be attributed to more common BME procedures, leading to earlier diagnosis and diagnosis of diseases. With the development of technology, invasive procedures are expected to decrease. These results need to be validated in larger study populations and different ethnic groups.

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